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Theoretical Study of the Anomeric Effect in CH_2ClOH

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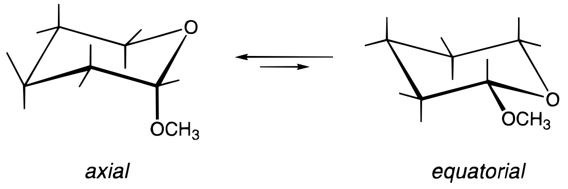
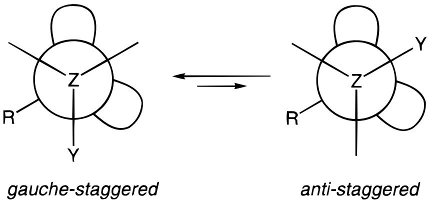
The anomeric effect has been analyzed theoretically by adopting a simple model molecule, CH_2ClOH. The total energy has been found at its minimum when the Cl−C−O−H dihedral angle is 66° (gauche-staggered conformation). By representing the wave function of the molecule in terms of the MOs of two fragments, we demonstrate that the oxygen p-type lone-pair orbital participates in electron donation to the C−Cl σ^* orbital in a wide range of the Cl−C−O−H dihedral angle. In contrast, a hybrid of s and p atomic orbitals of the oxygen interacts with the C−Cl σ^* orbital in the antiperiplanar (or anti-staggered) conformation. Electron delocalization is depressed in the anti conformation. The orbital interaction interprets consistently the shortened C−O bond and the elongated C−Cl bond in CH_2ClOH in the gauche-staggered conformation. The magnitude of the stabilization due to the effect has been estimated by using the fragment interaction orbitals, supporting the significance of electron delocalization in explaining the anomeric effect. The anomeric effect in the S_N2 reaction has also been studied.

Introduction

Edward reported in 1955 that the C(1) alkoxy group preferred the axial position to the equatorial position in a pyranose ring, despite unfavorable steric interactions with hydrogens at C(3) and C(5).[1] Lemieux and Chü observed the anomerization equilibria in several aldohexapyranoses and ascribed this phenomenon to a stereoelectronic control.[2] Similar observations have also been reported for six-membered pyranoses possessing electronegative substituents.[3−13] Now, these observations are explained in terms of the "anomeric effect".[14−25]

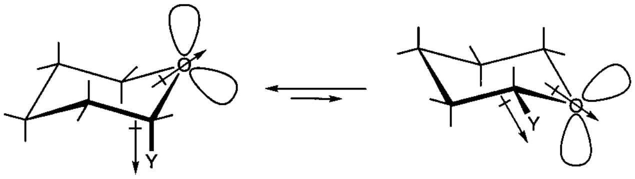


The same trend was also found in other cyclic rings[26−33] and in acyclic compounds.[34−37] Thus, the term "anomeric effect" has been generalized to refer to the gauche preference of electronegative substituents over the antiperiplanar conformation in an R−X−Z−Y moiety, in which Z is usually a carbon, Y denotes an atom more electronegative than Z, X represents an atom possessing lone pairs of electrons, and R stands for a hydrogen or an alkyl group.

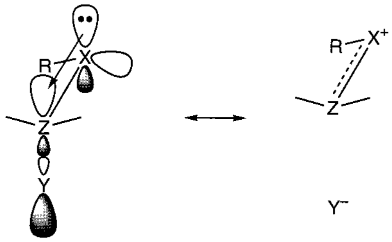


As for the origin of this effect, several explanations have been proposed by experimental and theoretical groups.[38−72] For example, Edward ascribed the axial preference of the group Y in a pyranose ring to the electrostatic repulsion between two dipole moments (Scheme 1).[1] The electrostatic model has been a subject of detailed discussions.[4−7,38,43,48,52a,58a,c,61,69a,b]

SCHEME 1



SCHEME 2



This model has been supported by some experimental results that advocate the decrease of the axial conformation ratio in polar solvents.[3b,38] It does not explain, on the other hand, the structural change observed in the axial conformation, such as the increase in the Z−Y bond length and the decrease in the X−Z bond length, and the opening of the Y−Z−X angle.[10a,26,31,37,53b−d,64,73−77] In addition, some experiments have reported the absence of any relation between the solvent polarity and the ratio of the axial conformation to the equatorial conformation.[43,44,48] To explain these observations, a stereoelectronic model has been proposed. This advocates the importance of delocalization of the lone pair of electrons on X to the Z−Y σ^* orbital. That is, negative hyperconjugation[65b] is of significance in making the axial conformation more stable relative to the equatorial conformation (Scheme 2).

The structural change in the axial conformation appears also to be interpreted by this stereoelectronic model. The validity

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of the model has been examined by many theoretical groups.[53a,54,56,57,60,62,64,65b,68] With regard to the energy of stabilization brought about by the anomeric effect, Schleyer and co-workers investigated several acyclic or cyclic compounds, applying the NBO analysis.[60c−e] They estimated the structural change due to the anomeric effect by measuring the differences between the optimized geometries at the full SCF level and those of the NBO Lewis structure. Radom and Pople studied the internal rotation of some acyclic compounds, such as ethane, methylamine, methanol, and fluoromethanol.[53a] The calculated energies were analyzed in terms of a Fourier-type expansion of the potential function, showing that the potential functions could be rationalized in terms of contributions from three principal effects. The 1-fold (V_1), 2-fold (V_2), and 3-fold (V_3) components expressed respectively the dipole−dipole repulsion, n−σ^* orbital interaction, and the steric factor. Then, Grein and Deslongchamps applied this analysis to acetals to study the origin of the anomeric effect.[68]

With a number of theoretical and experimental studies mentioned above, it has not been clarified yet what orbitals participate in the interaction between the lone pair of electrons and the antibonding σ^* orbital in α-halogenoethers having a chloroalkoxy group. We analyze in this study the orbital interactions in a CH_2ClOH molecule by applying our paired interaction orbital method.[78]

Computational Details

The structural optimization of CH_2ClOH has been carried out at the MP2(full)/6-311++G** level of theory by applying the Gaussian 94 program.[79] The interaction orbital analysis has been carried out with the RHF/6-31G** MOs of the optimized structures. The GAMESS program has been utilized to estimate the magnitude of stabilization brought about by the interaction between the lone-pair orbital of the oxygen and the σ^* orbital of the C−Cl bond in CH_2ClOH.[80]

Results and Discussion

Orbital Interactions. We have chosen in this study a simple molecule CH_2ClOH for an analysis of the anomeric effect. It is known well that 2-chlorooxane and its derivatives having a −CHClO− moiety manifest the anomeric effect very clearly.[13] To see if this molecule shows an anomeric effect proposed for α-halogenoethers, we have carried out geometry optimizations of a chloromethanol molecule, and also of the methanol, and chloromethane molecules at the MP2(full)/6-311++G** level of theory. Chloromethanol has been shown to prefer the gauche-staggered conformation with the Cl−C−O−H dihedral angle at 66° to the anti-staggered conformation, as illustrated in Figure 1. The C−O bond of CH_2ClOH in the gauche-staggered conformation has been calculated to be 0.1385 nm at the MP2(full)/6-31++G** level of theory, which is shorter than the C−O bond in methanol, by 0.0035 nm. On the other hand, the C−Cl bond of CH_2ClOH has been located at 0.1797 nm at the same level of calculation, which is 0.0022 nm longer than the C−Cl bond in chloromethane. These results indicate that this molecule should serve as the simplest model to analyze the origin of the anomeric effect.

We divide a CH_2ClOH molecule into two fragments, $(OH)^-$ and $(CH_2Cl)^+$, to look into the strength of electron delocalization across the C−O bond in this molecule. This division of the molecule into fragments is formal.[81] We utilize, however, the wave function of CH_2ClOH to draw the orbital interaction scheme between the fragments, and accordingly, the discussion of the anomeric effect should not be influenced by the partitioning of the molecule into fragments.

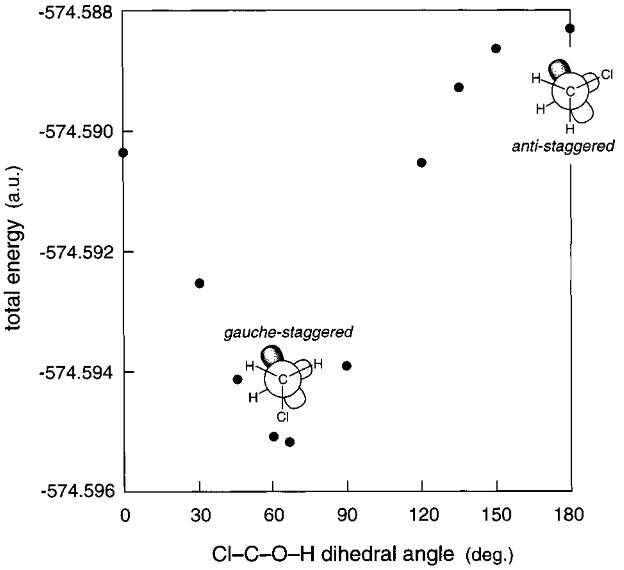

Figure 1. Change in the total energy of CH_2ClOH along with the rotation around the C−O bond.

We expand each MO of CH_2ClOH in terms of the MOs of the two fragments (LCMO)

$$\Phi_f = \sum_{i=1}^{m} c_{i,f}\phi_i + \sum_{j=m+1}^{M} c_{j,f}\phi_j + \sum_{k=1}^{N} d_{k,f}\psi_k + \sum_{l=n+1}^{N} d_{l,f}\psi_l \qquad (1)$$

where M and N indicate the number of the MOs of the $(OH)^-$ and $(CH_2Cl)^+$ fragments, respectively. The occupied and unoccupied MOs of $(OH)^-$ are denoted by ϕ_i (i = 1, 2, ..., m) and ϕ_j ($j = m + 1$, $m + 2$, ..., M), respectively, and the occupied and unoccupied MOs of the $(CH_2Cl)^+$ fragment are specified by ψ_k (k = 1, 2, ..., n) and ψ_l ($l = n + 1$, $n + 2$, ..., N), respectively. Now, we define a matrix **D** of the order ($M \times N$), by summing up the products of the LCMO coefficients between the two fragments, for instance, c_i for the MO ϕ_i of the $(OH)^-$ fragment and d_l for the MO ψ_l of the $(CH_2Cl)^+$ fragment, over all the occupied MOs of CH_2ClOH. We may employ the element D_{il} of this matrix as a scale of orbital interaction between the fragment MOs, ϕ_i and ψ_l. Among the orbital interactions between the two fragments, those between the occupied MOs of the donor part $(OH)^-$ and the unoccupied MOs of the acceptor part $(CH_2Cl)^+$ play crucial roles. Then, we have carried out transformations of the fragment orbitals within the occupied MO subspace of the donor part and the unoccupied MO subspace of the acceptor part, referring to the matrix **D**.[78] Now, electron delocalization from the $(OH)^-$ part to the $(CH_2Cl)^+$ part is represented concisely in terms of a few pairs of the occupied hybrid MOs of the former and the unoccupied hybrid MOs of the latter.

The strongest orbital interaction derived by this analysis is shown in Figure 2 for the most stable conformation of CH_2ClOH. We find an in-phase overlap between the interaction orbitals of the two fragments, pointing to each other. It is obvious that this pair stands for the C−O σ bond in CH_2ClOH that has been broken artificially upon dividing the molecule into two fragments. Very interestingly, the second orbital pair exhibits also an in-phase overlap between the two fragments, as illustrated in Figure 3. The orbital of the $(OH)^-$ fragment represents clearly one for a lone pair of electrons of the oxygen atom, and the paired counterpart of the $(CH_2Cl)^+$ fragment

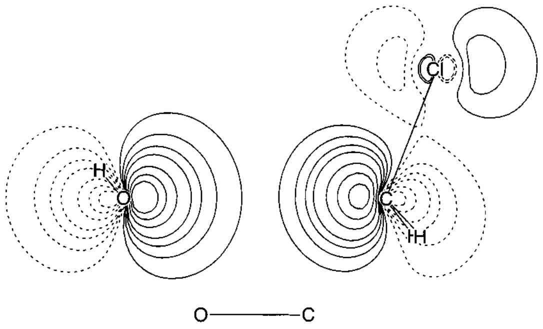

Figure 2. First pair of the interaction orbitals of the $(OH)^-$ and $(CH_2Cl)^+$ fragments, representing the formation of the C−O σ bond in CH_2ClOH.

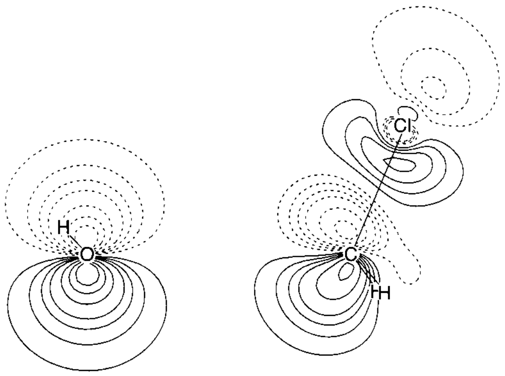

Figure 3. Second pair of the interaction orbitals of the $(OH)^-$ and $(CH_2Cl)^+$ fragments, representing electron delocalization from the oxygen to the C−Cl bond in the gauche-staggered conformation.

represents clearly the C−Cl σ^* orbital. It is suggested that this orbital pair gives rise to an anomeric effect in this species. Let us examine the role of the second orbital pair more in detail.

The Mulliken overlap population between the orbitals in the second pair has been shown to be at the maximum, 0.038, when the Cl−C−O−H dihedral angle θ is 90°, while it is at the minimum, 0.018, when the angle θ is 180°.[82] This seems to be in line with the result of a Fourier decomposition of the potential function for fluoromethanol,[53a] and also with the observation by Grein and Deslongchamps that the Mulliken charge of the OH group is smallest when the F−C−O−H dihedral angle is 90° in fluoromethanol.[68] The deviation of the most stable conformation ($\theta = 66°$) from the structure of the maximum overlap population may be attributed to the overlap repulsion between the lone pairs of electrons on the oxygen and the C−H bonds.

The explanation of the anomeric effect needs a clear understanding of the orbital for the lone pairs of electrons participating in the interaction with the C−Cl σ^* orbital. We have investigated the lone-pair orbital of the oxygen atom for several values of θ. At $\theta = 90°$, it is a pure p-type orbital of the oxygen that has an extension perpendicular to the C−O−H plane. In the structures with $\theta = 30-150°$, the p-character of the lone-pair orbital has been found to be very close to 100%. At $\theta = 60°$, for instance, the contribution of the s-type orbital has been calculated to be negligibly small (inner, 0%; outer, 2%).[83] Figure 3 illustrates that the orbital interaction takes place predominantly between the lone-pair orbital and the backside lobe of the C−Cl σ^* orbital, as has been assumed in Scheme 2.

In contrast, the contribution of the s-type atomic orbital is large in the anti-staggered conformation with $\theta = 180°$ (inner, 9%; outer, 66%).[83] This orbital is one of the hybrids constructed from the s and p atomic orbitals of the oxygen, the other two being used for the formation of the C−O and O−H bonds. The orbital is tilted backward and is delocalized to some extent over the adjacent hydrogen, as illustrated in Figure 4. A hybrid of the s and p atomic orbitals participates in the interaction with the C−Cl σ^* orbital in the anti-staggered conformation, and consequently, electron delocalization is suppressed. The molecule should be destabilized in this conformation, relative to the gauche-staggered conformation.

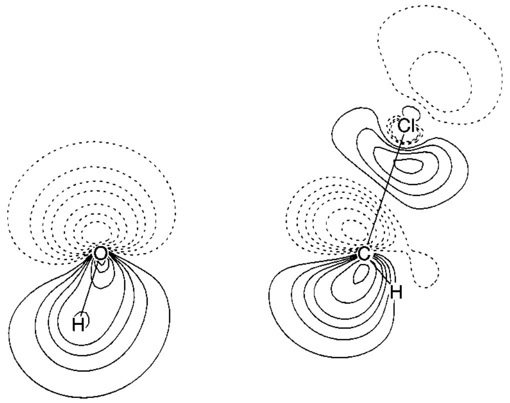

Figure 4. Second pair of the interaction orbitals of the $(OH)^-$ and $(CH_2Cl)^+$ fragments, representing electron delocalization from the oxygen to the C−Cl bond in the anti-staggered conformation.

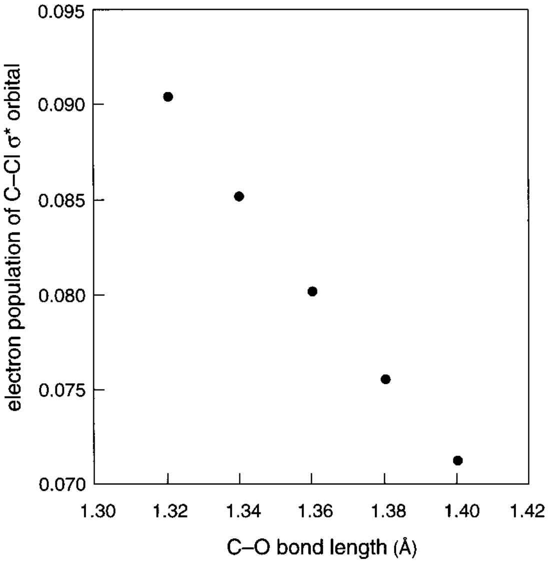

Figure 5. Change in the electron population of the C−Cl σ^* orbital associated with the lengthening of the C−O bond.

The C−Cl σ^* orbital is seen in Figures 3 and 4 to be distorted around the C−Cl bond to have a larger overlap with the oxygen lone-pair orbital. To see the effect of electron delocalization on the structural change in CH_2ClOH, we have investigated the relation between the electron population of the C−Cl σ^* orbital and the length of a C−O bond in a hypothetical molecule, in which θ is fixed at 90° and the C−Cl bond length is held at that in methyl chloride. Figure 5 shows that shortening of the C−O bond length leads to a higher electron population of the C−Cl σ^* orbital in the second pair of interaction orbitals, indicating that electron delocalization is pronounced as the C−O π-type overlap is strengthened.

We allowed next the C−Cl bond to change its length and studied the dependence of the C−Cl bond length on the electron population of the C−Cl σ^* orbital. It is seen in Figure 6 that the C−Cl bond is lengthened in proportion to the increase in

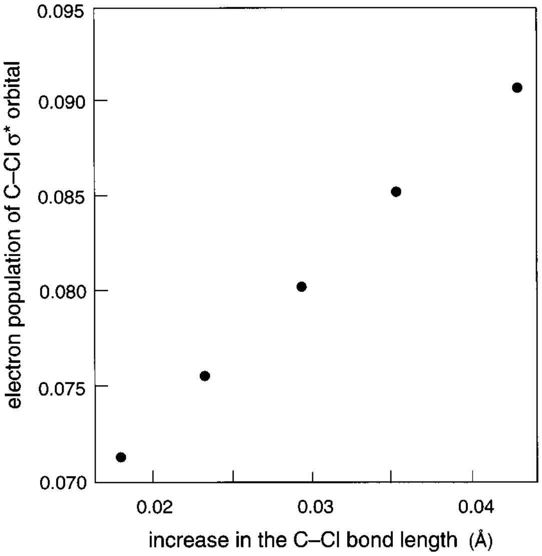

Figure 6. Change in the electron population of the C−Cl σ^* orbital associated with the lengthening of the C−Cl bond.

electron population of the orbital. The structural change in chloromethanol molecule is attributed to delocalization of the lone pair of electrons of the oxygen to the antibonding σ^* orbital of the C−Cl bond.

Strength of Electron Delocalization. The conclusion derived above from an analysis of orbital interactions appears to be very simple. A pure p-type lone-pair orbital participates in electron donation to the C−Cl σ^* orbital in the gauche-staggered conformation, whereas an s−p hybrid-type lone-pair orbital participates in electron donation in the anti-staggered conformation. Now, let us try to see numerically if the orbital interaction is strong enough to explain the gauche-staggered preference of the CH_2ClOH molecule. As shown above, each MO of the CH_2ClOH molecule has been rewritten in terms of a linear combination of the fragment orbitals. The Fock equations are also expressed in terms of these orbitals, giving the total energy E of the molecule. Then, the magnitude of conjugation between the lone-pair orbital of the oxygen and the σ^* orbital of the C−Cl bond in CH_2ClOH has been estimated in the following manner. We have deleted from the Fock equations the integrals that include both of the orbitals r and s, which denote respectively the orbital of the $(OH)^-$ fragment and the orbital of the $(CH_2Cl)^+$ fragment in the second orbital pair.[84] These integrals are not large in their magnitudes relative to those for the first pair of orbitals representing the C−O σ bond, and therefore, removal of these integrals does not affect seriously the electron distribution in a CH_2ClOH molecule.

By performing an SCF MO calculation on this system, we obtain the energy of the CH_2ClOH molecule, E'. Figure 7 illustrates $E' - E$ calculated at the 6-31G** level of theory. This energy difference is regarded as giving the stabilization due to the anomeric effect. The stabilization is at its maximum when θ is 90°. This stabilization is counterbalanced in part by overlap repulsion between the O−H bond and the C−H and C−Cl bonds and between the lone pairs of electrons of the oxygen and the C−H and C−Cl bonds, and locates the most stable conformation of the CH_2ClOH molecule not at $\theta = 60°$, but at a somewhat larger Cl−C−O−H dihedral angle, 66°, as has been illustrated in Figure 1. The energy difference ($E' - E$) is 15−20 kJ/mol greater in the range $\theta = 60{-}100°$, compared with that for the anti-staggered conformation. This seems to be in agreement with the value 24 kJ/mol, evaluated from the methyl stabilization energy in the reaction $XCH_2Y + CH_4 \rightarrow CH_3X + CH_3Y$.[60b] The most stable conformation of CH_2ClOH may also be influenced by some other factors, such as electron delocalization from the oxygen lone-pair orbitals to the C−H σ^* orbitals. Considering, however, that the energy difference between the gauche-staggered and anti-staggered conformations is 19.3 and 18.0 kJ/mol at the RHF/6-31G** and MP2(full)/6-311++G** level of theory, respectively, the strength of the orbital interaction found in this study should be of significance and reasonable in its magnitude in understanding the preference of the gauche-staggered conformation in CH_2ClOH.

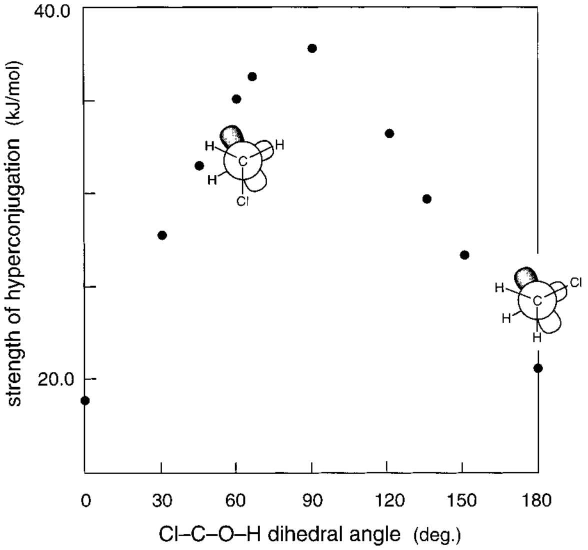

Figure 7. Effect of the orbital interaction between the oxygen lone pair of electrons and the C−Cl σ^* orbital upon the total energy of CH_2ClOH.

TABLE 1: Effect of the Cl−C−O−H Dihedral Angle on the Reactivity of Chloromethanol with Cloride Anion

Cl−C−O−H dihedral angle (deg)	activation energy (kJ/mol)[a]	anomeric effect (kJ/mol)
0	27.8	48.0
0	26.7	65.9
60	21.8	102.3
90	15.5	112.7

[a] MP2(full)/6-311++G**.

Anomeric Effect in S_N2 Transition States. The rate of bimolecular nucleophilic substitution reactions has been shown to be highly enhanced in α-halogenoethers.[15] This enhancement occurs only when the lone pair of electrons of the oxygen comes antiperiplanar to the C−X bond. It has been assumed, therefore, that the anomeric interaction between the oxygen and the reaction center plays a significant role in stabilizing the transition state. To see the orbital interaction, we have adopted a system composed of chloromethanol and chloride anion as a reaction model and have carried out the MO calculations on an imaginary system in which the Cl−C−O−H dihedral angle of chloromethanol is fixed at several values through the entire reaction path. The activation energy calculated in this manner is presented in Table 1. One sees that the barrier height is the lowest at 90°. This result implies that the orientation of the lone pair of electrons of the oxygen affects strongly the reactivity of chloromethanol in the S_N2 reaction. To see further the conjugation, we divided the reaction system [Cl- - -CH_2- - -ClOH] at the transition states into two fragments, $[OH]^-$ and [Cl- - -CH_2- - -Cl], and applied the paired interaction orbital scheme explained above. When the dihedral angle is 90°, the lone pair of electrons on the oxygen is shown to delocalize efficiently

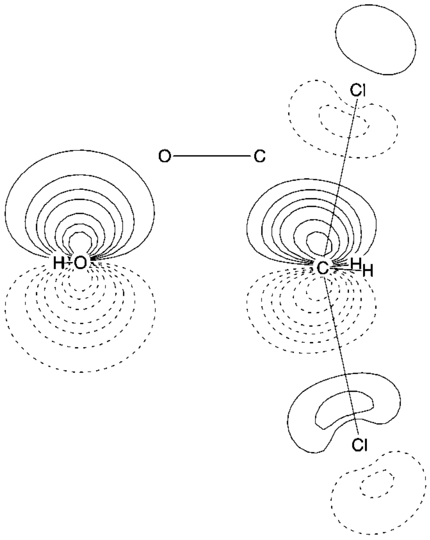

Figure 8. Interaction orbitals of the $(OH)^-$ and $(ClCH_2Cl)$ fragments, taking part in electron delocalization from the lone-pair orbital of OH^- to the Cl- - -C- - -Cl bonds at the transition state of the S_N2 reaction of chloromethanol with the chloride ion.

over the reaction center through the overlap with the Cl- - -C- - -Cl three-centered antibonding orbital, as illustrated in Figure 8. When we do not impose any geometrical constraint on the reaction system, the dihedral angle is calculated to be very close to 90° at the transition state. It is concluded, therefore, that the anomeric effect contributes to the stabilization of the transition state.

To see if this orbital interaction really dominates the reactivity of chloromethanol, we have estimated the stabilization due to the orbital interaction. Interestingly, the stabilization becomes stronger as the dihedral angle reaches 90°, as shown in Table 1. Incidentally, the orbital interaction between the lone-pair orbital of the attacking chloride ion and the C−Cl σ^* orbital of chloromethanol has been shown to remain within 59−68 kJ/mol for the dihedral angle of 0−90°. The stabilization due to the anomeric effect should be counterbalanced in part by the repulsive interaction between the lone pair of electrons on the oxygen and the electrons in the C−Cl bonds.

Conclusion

We have studied the anomeric effect in a simple model molecule, CH_2ClOH. By dividing the CH_2ClOH molecule into two fragments, $(OH)^-$ and $(CH_2Cl)^+$, we have clearly illustrated the delocalization of the oxygen lone pair of electrons to the C−Cl bond by means of a pair of interaction orbitals of the fragments. In a relatively wide range of the Cl−C−O−H dihedral angle, the oxygen orbital participating in electron delocalization has been shown to be of pure p-character. In contrast, in the anti-staggered conformation, an s−p hybrid of oxygen has been demonstrated to participate in electron delocalization. The orbital interaction should be weaker in the anti-staggered conformation. Electron delocalization between the two fragments interprets successfully the shortened C−O bond and the elongated C−Cl bond in CH_2ClOH. The effect of orbital interactions on the conformational energy change has been evaluated by combining the MO theory and the interaction orbital scheme, providing the value of 19−38 kJ/mol in the range $\theta = 0-180°$. Thus, evidence that supports the importance of electron delocalization in generating the anomeric effect has been obtained with a clear view of orbital interactions involved in CH_2ClOH. The anomeric effect is suggested to play a significant role in enhancing the reactivity of α-halogenoethers for bimolecular nucleophilic substitution reactions.

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References and Notes

(1) Edward, J. T. *Chem. Ind.* **1955**, 1102.

(2) (a) Lemieux, R. U.; Chü, N. J. *Abstr. Pap., Am. Chem. Soc.* **1958**, *133*, S31N. (b) Praly, J. D.; Lemieux, R. U. *Can. J. Chem.* **1987**, *65*, 213.

(3) (a) Eliel, E. L. *Angew. Chem.* **1965**, *77*, 784. (b) Eliel, E. L.; Giza, C. A. *J. Org. Chem.* **1968**, *33*, 3754. (c) Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635.

(4) (a) Booth, G. E.; Ouellette, R. J. *J. Org. Chem.* **1966**, *31*, 544. (b) Booth, H.; Grindley, T. B.; Khedhair, K. A. *J. Chem. Soc., Chem. Commun.* **1982**, 1047.

(5) Pierson, G. O.; Runquist, O. A. *J. Org. Chem.* **1968**, *33*, 2572.

(6) de Hoog, A. T.; Buys, H. R.; Altona, C.; Havinga, E. *Tetrahedron* **1969**, *25*, 3365.

(7) Anderson, C. B.; Sepp, D. T. *Tetrahedron* **1968**, *24*, 1707.

(8) Bailey, W. F.; Eliel, E. L. *J. Am. Chem. Soc.* **1974**, *96*, 1798.

(9) Franck, R. W. *Tetrahedron* **1983**, *39*, 3251.

(10) (a) Briggs, A. J.; Glenn, R.; Jones, P. G.; Kirby, A. J.; Ramaswamy, P. *J. Am. Chem. Soc.* **1984**, *106*, 6200 and references therein. (b) Jones, P. G.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6207.

(11) Perrin, C. L.; Nuñez, O. *J. Chem. Soc., Chem. Commun.* **1984**, 333.

(12) (a) Booth, H.; Khedhair, K. A. *J. Chem. Soc., Chem. Commun.* **1985**, 467. (b) Booth, H.; Khedhair, K. A.; Readshaw, S. A. *Tetrahedron* **1987**, *43*, 4699. (c) Booth, H.; Dixon, J. M.; Khedhair, K. A.; Readshaw, S. A. *Tetrahedron* **1990**, *46*, 1625.

(13) Lichtenthaler, F. W.; Rönninger, S.; Kreis, U. *Liebigs Ann. Chem.* **1990**, 1001.

(14) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag; Berlin, 1983.

(15) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Wiley: New York; 1983.

(16) Thatcher, C. R. J., Ed. *The Anomeric Effect and Associated Stereoelectronic Effects*, A. C. S. Symposium Series No. 539; American Chemical Socoety: Washington, DC. 1993.

(17) Lemieux, R. U. In *Molecular Rearrangements*; de Mayo, P., Ed.; Interscience: New York; 1964; Vol.3, p 709.

(18) Eliel, E. L. *Acc. Chem. Res.* **1970**, *3*, 1.

(19) Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102.

(20) Deslongchamps, P. *Tetrahedron* **1975**, *31*, 2463.

(21) Tvaroška, I.; Bleha, T. In *Advances in Carbohydrate Chemistry and Biochemistry*; Tipson, R. S., Horton, D., Eds.; Academic Press: San Diego, 1989; p 45.

(22) Box, V. G. S. *Heterocycles* **1990**, *31*, 1157.

(23) Gorenstein, D. G. *Chem. Rev.* **1987**, *87*, 1047.

(24) Juaristi, E.; Cuevas, G. *Tetrahedron* **1992**, *48*, 5019.

(25) Kirby, A. J. *Stereoelectronic Effects*; Oxford Science Publishers: Oxford, U.K., 1996.

(26) Hilling, K. W., II; Lattimer, R. P.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1982**, *104*, 988.

(27) Jørgensen, F. S.; Nørskov-Lauristen, L. *Tetrahedron Lett.* **1982**, *23*, 5221.

(28) Fuchs, B.; Ellencweig, A.; Burkert, U. *Tetrahedron* **1984**, *40*, 2011.

(29) Aped, P.; Apeloig, Y.; Ellencweig, A.; Fuchs, B.; Goldberg, I.; Karni, M.; Tartakovsky, E. *J. Am. Chem. Soc.* **1987**, *109*, 1486.

(30) (a) Cossé-Barbi, A.; Dubois, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 1503. (b) Cossé-Barbi, A.; Watson, D. G.; Dubois, J. E. *Tetrahedron Lett.* **1989**, *30*, 163.

(31) LaBarge, M. S.; Keul, H.; Kuczkowski, R. L.; Wallasch, M.; Cremer, D. *J. Am. Chem. Soc.* **1988**, *110*, 2081.

(32) Leroy, G.; Dewispelaere, J. P.; Benkadour, H.; Temsamani, D. R.; Wilante, C. *J. Mol. Struct.* **1995**, *334*, 137.

(33) Suárez, D.; Sordo, L. T.; Sordo, A. J. *J. Am. Chem. Soc.* **1996**, *118*, 9850.

(34) Planje, M. C.; Toneman, L. H.; Dallinga, G. *Recl. Trav. Chim.* **1963**, *82*, 1080.

(35) (a) Anet, F. A. L.; Yavari, I. *J. Am. Chem. Soc.* **1977**, *99*, 6752. (b) Anet, F. A. L.; Kopelevich, M. *J. Am. Chem. Soc.* **1986**, *108*, 210.

(36) Kost, D.; Raban, M. *J. Am. Chem. Soc.* **1982**, *104*, 2960.

(37) Narasimhamurthy, N.; Manohar, H.; Samuelson, A.; Chandrasekhar, J. *J. Am. Chem. Soc.* **1990**, *112*, 2937.

(38) Lemieux, R. U.; Pavia, A. A.; Martin, J. C.; Watanabe, K. A. *Can. J. Chem.* **1969**, *47*, 4427.

(39) Eliel, E. L.; Rao, V. S.; Vierhapper, F. W.; Juaristi, G. Z. *Tetrahedron Lett.* **1975**, 4339.

(40) Jones, P. G.; Kirby, A. J. *J. Chem. Soc., Chem. Commun.* **1979**, 288.

(41) Fraser, R. R.; Bresse, M. *Can. J. Chem.* **1983**, *61*, 576.

(42) Zefirov, N. S.; Baranenkov, I. V. *Tetrahedron* **1983**, *39*, 1769.

(43) Fuchs, B.; Ellencweig, A.; Tartakovsky, E.; Aped, P. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 287.

(44) Juaristi, E.; Tapia, J.; Méndez, R. *Tetrahedron* **1986**, *42*, 1253.

(45) Penner, G. H.; Schaefer, T.; Sebastian, R.; Wolfe, S. *Can. J. Chem.* **1987**, *65*, 1845.

(46) Ouedraogo, A.; Viet, M. T. P.; Saunders, J. K.; Lessard, J. *Can. J. Chem.* **1987**, *65*, 1761.

(47) Sinnot, M. L. *Adv. Phys. Org. Chem.* **1988**, *24*, 113.

(48) Pinto, B. M.; Johnston, B. D.; Nagelkerke, R. *J. Org. Chem.* **1988**, *53*, 5668.

(49) Bailey, W. F.; Rivera, A. D.; Rossi, K. *Tetrahedron Lett.* **1988**, *29*, 5621.

(50) Carr, C. A.; Ellison, S. L. R.; Robinson, M. J. T. *Tetrahedron Lett.* **1989**, *30*, 4585.

(51) Denmark, S. E.; Dappen, M. S.; Sear, N. L.; Jacobs, R. T. *J. Am. Chem. Soc.* **1990**, *112*, 3446.

(52) (a) Wolfe, S.; Rauk, A.; Tel, L. M.; Csizmadia, I. G. *J. Chem. Soc. B* **1971**, 136. (b) Wolfe, S.; Whangbo, M.-H.; Mitchell, D. J. *Carbohydr. Res.* **1979**, *69*, 1.

(53) (a) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 2371. (b) Jeffrey, G. A.; Pople, J. A.; Radom, L. *Carbodydr. Res.* **1972**, *25*, 117. (c) Jeffrey, G. A.; Pople, J. A.; Radom, L. *Carbohydr. Res.* **1974**, *38*, 81. (d) Jeffrey, G. A.; Pople, J. A.; Binkley, J. S.; Vishveshwara, S. *J. Am. Chem. Soc.* **1978**, *100*, 373.

(54) (a) David, S.; Eisenstein, O.; Hehre, W. J.; Salem, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1973**, *95*, 3806. (b) Eisenstein, O.; Anh, N. T.; Jean, Y.; Devaquet, A.; Catacuzene, J.; Salem, L. *Tetrahedron* **1974**, *30*, 1717.

(55) (a) Lehn, J. M.; Wipff, G.; Bürgi, H. B. *Helv. Chim. Acta* **1974**, *57*, 491. (b) Wipff, G. *Tetrahedron Lett.* **1978**, *35*, 3269. (c) Lehn, J. M.; Wipff, G. *J. Am. Chem. Soc.* **1980**, *102*, 1347.

(56) Bingham, R. C. *J. Am. Chem. Soc.* **1975**, *97*, 6743.

(57) Epiotis, N. D.; Yates, R. L.; Bernardi, F.; Wolfe, S. *J. Am. Chem. Soc.* **1976**, *98*, 5435.

(58) (a) Tvaroška, I.; Kožár, T. *J. Am. Chem. Soc.* **1980**, *102*, 6929. (b) Tvaroška, I.; Kožár, T. *Carbohydr. Res.* **1981**, *90*, 173. (c) Tvaroška, I.; Kožár, T. *Int. J. Quantum. Chem.* **1983**, *23*, 765.

(59) Vishveshwara, S.; Rao, V. S. R. *Carbohydr. Res.* **1982**, *104*, 21.

(60) (a) Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141. (b) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393. (c) Reed, A. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1987**, *109*, 7362. (d) Salzner, U.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1993**, *115*, 10231. (e) Salzner, U.; Schleyer, P. v. R. *J. Org. Chem.* **1994**, *59*, 2138.

(61) Gresh, N.; Claverie, P.; Pullman, A. *Theor. Chim. Acta* **1984**, *66*, 1.

(62) Magnusson, E. *J. Am. Chem. Soc.* **1986**, *108*, 11.

(63) Inagaki, S.; Iwase, K.; Mori, Y. *Chem. Lett.* **1986**, 417.

(64) Pinto, B. M.; Schlegel, H. B.; Wolfe, S. *Can. J. Chem.* **1987**, *65*, 1658.

(65) (a) Wiberg, K. B.; Murcko, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 4821. (b) Wiberg, K. B.; Rablen, P. R. *J. Am. Chem. Soc.* **1993**, *115*, 614.

(66) (a) Senderowitz, H.; Aped, P.; Fuchs, B. *Helv. Chim. Acta* **1990**, *73*, 2113. (b) Senderowitz, H.; Aped, P.; Fuchs, B. *Tetrahedron* **1992**, *48*, 1131. (c) Senderowitz, H.; Aped, P.; Fuchs, B. *Tetrahedron* **1993**, *49*, 3879. (d) Ganguly, B.; Fuchs, B. *J. Org. Chem.* **1997**, *62*, 8892. (e) Schleifer, L.; Senderowitz, H.; Aped, P.; Tartakovsky, E.; Fuchs, B. *Carbohydr. Res.* **1990**, *206*, 21.

(67) Irwin, J. J.; Ha, T.-K.; Dunitz, J. D. *Helv. Chim. Acta* **1990**, *73*, 1805.

(68) Grein, F.; Deslongchamps, P. *Can. J. Chem.* **1992**, *70*, 604.

(69) (a) Cramer, C. J. *J. Org. Chem.* **1992**, *57*, 7034. (b) Cramer, C. J.; Truhlar, D. G. *J. Am. Chem. Soc.* **1993**, *115*, 5745.

(70) Jorgensen, W. L.; Molares de Tirado, P. I.; Severance, D. L. *J. Am. Chem. Soc.* **1994**, *116*, 2199.

(71) Srivastava, R. M.; Pavão, A. C.; Seabra, G. M.; Brown, R. K. *J. Mol. Struct.* **1997**, *412*, 51.

(72) Marcos, E. S.; Pappalardo, R. R.; Chiara, J. L.; Domeme, M. C.; Martinez, J. M.; Parrondo, R. M. *J. Mol. Struct.* (*THEOCHEM*) **1996**, *371*, 245.

(73) McDonald, T. R.; Beevers, C. A. *Acta Crystallogr.* **1952**, *5*, 654.

(74) Berman, H. M.; Chu, S. S. C.; Jeffrey, G. A. *Science* **1967**, *157*, 1576.

(75) Arnott, S.; Scott, W. E. *J. Chem. Soc., Perkin Trans.* 2. **1972**, 324.

(76) Perez, S.; Marchessault, R. H. *Carbohydr. Res.* **1978**, *65*, 114.

(77) Laing, M. *J. Chem. Educ.* **1987**, *64*, 124.

(78) (a) Fukui, K.; Koga, N.; Fujimoto, H. *J. Am. Chem. Soc.* **1981**, *103*, 196. (b) Fujimoto, H.; Koga, N.; Fukui, K. *J. Am. Chem. Soc.* **1981**, *103*, 7452. (c) Fujimoto, H.; Hataue, I.; Koga, N. *J. Phys. Chem.* **1985**, *89*, 779.

(79) Frish, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Ciolowski, J.; Stefanov, B. B.; Nanayakkara, A.; Chalacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94*; Gaussian Inc.: Pittsburgh, PA, 1995.

(80) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.

(81) A configuration analysis has shown that the $[(CH_2Cl)^+ + (OH)^-]$ configuration has approximately the same energy as the $[(CH_2Cl)^\bullet + (OH)^\bullet]$ singlet electron configuration, in which an electron has been shifted from the interaction orbital of the $(CH_2Cl)^+$ fragment to the interaction orbital of the $(OH)^-$ fragment in the first pair of orbitals, shown in Figure 2 (for configuration analysis, see: Fujimoto, H.; Kato, S.; Yamabe, S.; Fukui, K. *J. Chem. Phys.* **1974**, *60*, 572). Thus, we may start our analysis of the orbital interaction either from the $[(CH_2Cl)^+ + (OH)^-]$ electron configuration or from the $[(CH_2Cl)^\bullet + (OH)^\bullet]$ configuration. This was confirmed also by analyzing the restricted Hartree−Fock open-shell MOs of the two radical fragments.

(82) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.

(83) Estimated by the square of the AO coefficients in the interaction orbital.

(84) By simply placing the conditions, $F_{rs} = 0$, $S_{rs} = 0$, and $h_{rs} = 0$ (see for example: Kitaura, K.; Morokuma, K. *Int. J. Quantum Chem.* **1976**, *10*, 325) for the second orbital pair (r, s), we show the anomeric effect to be strongest at $\theta = 106°$ in the present system. The stabilization energy obtained by this scheme appears to be too large, being 38 kJ/mol above the value at $\theta = 180°$ and 88 kJ/mol above the value at $\theta = 0°$. Removal of the orbital interactions between the occupied MOs of one fragment, A, and the unoccupied MOs of the other fragment, B, will lead, at the same time, to the depression of electron delocalization from B to A, by reducing the electron-accepting ability of A and the electron-donating ability of B.